35 USC § 103 Obviousness Rejection

"Claims 1-4, 6,7,and 8-19 are rejected and it said that it would have been obvious to optimize the steps of Reeve (U.S. Patent No. 5,800,711) to enhance separation."

U.S. Patent No. 5,800,711 discloses a conventional extraction method to fractionate polyoxyalkylene polymers using an organic solvent in water and a salt. Such methods separate mixtures of molecules primarily on the differing polarities of the molecules in the mixture. The specification defines the water/organic extraction solvent as "any solvent that remains miscible in the water/organic/salt system" (Column 5, 49-60). The best mode for both poloxamers 407 and 188 is 75/25 water/n-propanol (Examples 1-5).

The present invention discloses a separation method based on an aqueous two phase system. This method does not require the limitation of having a water miscible organic solvent in the extraction medium.

U.S. Patent No. 5,800,711 discloses use of soluble organic salts defined as "any halide, acetate, hydroxide, carbonate, sulfate, or phosphate salt of the alkali or alkaline-earth metals from groups IA and IIA of the periodic table" (ie, mono-, or divalent salts), sodium chloride (monovalent) being the preferred salt.

The present invention uses salt to facilitate phase separation. However, as described in the Hatti-Kaul reference, the relative effectiveness of various salts in promoting phase separation follows the Hofmeister series, and multivalent anions such as HPO_4^{2-} and SO_4^{2-} are most effective in inducing phase separation ("Aqueous Two-Phase Systems", Rajni Hatti-Kaul, ed., p. 2, first paragraph.). In the present invention, the preferred salt is ammonium sulfate. Sodium chloride, being monovalent, is not efficacious. The claims have been amended to reflect the preference for multivalent salts.

Aqueous two-phase systems have been used to separate a range of biomaterials including plant and animal cells, microorganisms, fungi and their spores, viruses, chloroplasts, mitochondria, membrane vesicles, proteins, and nucleic acids ("Aqueous Two-Phase Systems, Rajni Hatti-Kaul, ed., p 2, paragraph 3). Of these biomaterials, proteins and nucleic acid polymers may be man-made, and therefore considered synthetic, and clearly prior art, as conceded on page 7 of the specification of the present application. However, no one has used an aqueous two-phase system to fractionate polyethers or polyols such as the polyethylene glycol(s), polyoxyalkylene polymers, or polyvinyl alcohol polymers. Claim 1 has been amended to distinguish between synthetic proteins and nucleic acids, and synthetic polyethers and polyols.

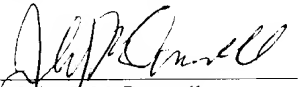
The polyoxyalkylene block copolymers are composed of polyoxypropylene and polyoxyethylene subunits. Because polyoxypropylene is less polar than polyoxyethylene, individual polyoxyalkylene molecules differ in polarity based on their content of each subunit. The fractionation of the

polyoxyalkylene block copolymers disclosed in U.S. Patent 5,800,711 exploits the polarity differences among large and small molecules. In contrast, polyethylene glycol is a homopolymer composed only of ethylene glycol subunits. The only difference between individual molecules of polyethylene glycol is molecular weight. Therefore, the fractionation obtained in the present application is achieved by adjusting the concentrations of the polymer to be fractionated and the multivalent salt and the temperature so that lower molecular weight molecules partition into one phase and higher molecular weight molecules partition into the other phase. Thus, the aqueous two-phase system is distinctly different from conventional extraction methods using organic solvents. Other differences between the two methods are described in "Aqueous Two-Phase Systems", Rajni Hatti-Kaul, ed., p 2 paragraph 3, indicating that the two systems are generally considered distinct from each other. Therefore, the separation method of the present invention, based on an aqueous two-phase system and developed for the fractionation of synthetic polyethers and polyols, is not obvious and is distinct from the conventional extraction method disclosed in U.S. Patent 5,800,711, and not a routine optimization of it.

It is respectfully submitted that the claims are not obvious in view of the 5,800,711 alone or in combination with other references.

Allowance of the claims is earnestly solicited.

Respectfully submitted,

By: 

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